

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of inhibiting zinc release from neurons, comprising: providing to said neurons at least one agent that inhibits nitric oxide synthesis to reduce the level of nitric oxide sufficiently to inhibit release of zinc from said neurons, ~~and reducing levels of nitric oxide that induce release of zinc thereby inhibiting release of zinc from said neurons.~~

2 (Original) The method of claim 1, wherein said zinc is located in pre-synaptic vesicles, in post-synaptic zinc sequestering proteins, or in mitochondrial stores in post-synaptic neurons, or a combination thereof.

3 (Original) The method of claim 1, wherein said agent(s) inhibits the activity of neuronal nitric oxide synthase, inducible nitric oxide synthase or a combination thereof.

4 (Currently Amended) The method of claim 1, wherein said agent is 7-nitroindazole, S-methyl-1-thiocitrulline, the protein PIN, 2-amino-5,6-methyl-4H-1,3-thiazine, N(6)-iminoethyl-L-lysine, ~~N(6)-iminoethyl-L-lysine~~, N-(3-aminomethyl)benzyl acetamidine, or S-[2-amino-(1-iminoethylamino)5-thioheptanoic acid].

5 (Currently Amended) The method of claim 1, wherein inhibition of zinc release ~~prevents~~ reduces a zinc-mediated brain injury.

6 (Original) The method of claim 5, wherein said zinc-mediated brain injury is caused by stroke, head trauma, ischemia, seizure, or surgery comprising cerebral blood flow.

7 (Withdrawn) A method of preventing zinc-mediated brain injury, comprising: administering to an individual susceptible to trauma-induced excitotoxicity one or more first agent(s) that inhibits nitric oxide synthesis; and reducing nitric oxide-induced release of zinc from neuronal cells in response to said trauma-induced excitotoxicity thereby preventing zinc-mediated brain injury.

8 (Withdrawn) The method of claim 7, wherein said first agent inhibits nitric oxide synthetic activity of neuronal nitric oxide synthase, of inducible nitric oxide synthase, of both neuronal nitric oxide synthase and inducible nitric oxide synthase or a combination thereof.

9 (Withdrawn) The method of claim 7, wherein said first agent is 7-nitroindazole, S-methyl-1-thiocitrulline, the protein PIN, 2-amino-5,6-methyl-4H-1,3-thiazine, N(6)-iminoethyl-L-lysine, N(6)-iminoethyl-L-lysine, N-(3-aminomethyl)benzyl acetamidine, or S-[2-amino-(1-iminoethylamino)5-thioheptanoic acid].

10 (Withdrawn) The method of claim 5, further comprising:
administering a second agent to improve cerebral blood flow, said second agent different from said first agent.

11 (Withdrawn) The method of claim 10, wherein said second agent increases the activity of endothelial nitric oxide synthase.

12 (Withdrawn) The method of claim 11, wherein said second agent is simvastatin, 17-beta-estradiol, a corticosteroid, endothelin, or AT2 receptor agonists.

13 (Withdrawn) The method of claim 12, wherein said corticosteroid is dexamethasone.

14 (Withdrawn) The method of claim 10, wherein said second agent is a pressor.

15 (Withdrawn) the method of claim 14, wherein said pressor is dopamine, vasopressin, angiotensin II, or epinephrine.

16 (Withdrawn) The method of claim 7, wherein release of said excitotoxic zinc is caused by stroke, head trauma, ischemia, seizure, or surgery compromising cerebral blood flow.

17 (Withdrawn) The method of claim 16, wherein said surgery is cardiobypass, cardiopulmonary bypass, or carotid endarterectomy.

18 (Withdrawn) The method of claim 7, wherein said excitotoxic zinc is released from pre-synaptic vesicles, post-synaptic zinc sequestering proteins or mitochondrial stores in the post-synaptic neurons.

19 (Withdrawn) The method of claim 7, wherein said surgery is selected from the group consisting of cardiac bypass and carotid endarterectomy.

20 (Withdrawn) A method of improving cerebral blood flow while preventing zinc-mediated brain injury in an individual in need of such therapeutic intervention, comprising:

administering to said individual an agent(s) that inhibits one or both of neuronal nitric oxide synthase and inducible nitric oxide synthase, and
administering an agent that increases the activity of endothelial nitric oxide synthase;
wherein the combination of said agents modulates the nitric oxide synthesis in said individual such that the nitric oxide synthesized improves the cerebral blood flow, but said nitric oxide does not induce release of neurotoxic amounts of zinc thereby preventing zinc-mediated brain injury.

21. (Withdrawn) The method of claim 20, wherein said agent inhibiting nNOS or iNOS is 7-nitroindazole, S-methyl-1-thiocitrulline, the protein PIN, 2-amino-5,6-methyl-4H-1,3-thiazine, N(6)-iminoethyl-L-lysine, N(6)-iminoethyl-L-lysine, N-(3-aminomethyl)benzyl acetamidine, or S-[2-amino-(1-iminoethylamino)5-thioheptanoic acid].

22 (Withdrawn) The method of claim 20, wherein said agent increasing the activity of eNOS is simvastatin, 17-beta-estradiol, a corticosteroid, endothelin, or AT2 receptor agonists.

23 (Withdrawn) The method of claim 22, wherein said corticosteroid is dexamethasone.

24 (Withdrawn) The method of claim 20, wherein said zinc-mediated brain injury is caused by stroke, head trauma, ischemia, seizure, or surgery that would compromise cerebral blood flow.

25 (Withdrawn) The method of claim 24, wherein said surgery is cardiobypass, cardiopulmonary bypass or carotid endarterectomy.

26 (Withdrawn) The method of claim 20, wherein said neurotoxic zinc is released from pre-synaptic vesicles, post-synaptic zinc sequestering proteins or mitochondrial stores in the post-synaptic neurons.

27 (Withdrawn) The method of claim 20, wherein said agents are administered in a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

28 (Withdrawn) A method of improving cerebral blood flow while preventing zinc-mediated brain injury in an individual in need of such therapeutic intervention, comprising:
administering to said individual an agent(s) that inhibits one or both of neuronal nitric oxide synthase and inducible nitric oxide synthase, and in combination
administering a pressor;

wherein said pressor improves cerebral blood flow as said agent(s) reduces nitric oxide-induced release of neurotoxic zinc thereby preventing zinc-mediated brain injury.

29 (Withdrawn) the method of claim 28, wherein said agent inhibiting nNOS or iNOS is 7-nitroindazole, S-methyl-1-thiocitrulline, the protein PIN, 2-amino-5,6-methyl-4H-1,3-thiazine, N(6)-iminoethyl-L-lysine, N(6)-iminoethyl-L-lysine, N-(3-aminomethyl)benzyl acetamidine, or S-[2-amino-(1-iminoethylamino)5-thioheptanoic acid].

30 (Withdrawn) The method of claim 28, wherein said pressor is dopamine, vasopressin, angiotensin II, or epinephrine.

31 (Withdrawn) The method of claim 28, wherein said zinc-mediated brain injury is caused by stroke, head trauma, ischemia, seizure, or surgery that would compromise cerebral blood flow.

32 (Withdrawn) The method of claim 31, wherein said surgery is cardiobypass, cardiopulmonary bypass or carotid endarterectomy.

33 (Withdrawn) The method of claim 28, wherein said neurotoxic zinc is released from pre-synaptic vesicles, post-synaptic zinc sequestering proteins or mitochondrial stores in the post-synaptic neurons.

34 (Withdrawn) The method of claim 28, wherein said agent(s) and said pressor are administered in a pharmaceutical composition comprising a pharmaceutically acceptable carrier.